

Home Oxygen Therapy for Children

An Official American Thoracic Society Clinical Practice Guideline: Executive Summary

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THIS OFFICIAL CLINICAL PRACTICE GUIDELINE OF THE AMERICAN THORACIC SOCIETY WAS APPROVED DECEMBER 2018

Background: Home oxygen therapy is often required in children with chronic respiratory conditions. This document provides an evidence-based clinical practice guideline on the implementation, monitoring, and discontinuation of home oxygen therapy for the pediatric population.

Methods: A multidisciplinary panel identified pertinent questions regarding home oxygen therapy in children, conducted systematic reviews of the relevant literature, and applied the Grading of Recommendations, Assessment, Development, and Evaluation approach to rate the quality of evidence and strength of clinical recommendations.

Results: After considering the panel's confidence in the estimated effects, the balance of desirable (benefits) and undesirable (harms and burdens) consequences of treatment, patient values and preferences,

cost, and feasibility, recommendations were developed for or against home oxygen therapy specific to pediatric lung and pulmonary vascular diseases.

Conclusions: Although home oxygen therapy is commonly required in the care of children, there is a striking lack of empirical evidence regarding implementation, monitoring, and discontinuation of supplemental oxygen therapy. The panel formulated and provided the rationale for clinical recommendations for home oxygen therapy based on scant empirical evidence, expert opinion, and clinical experience to aid clinicians in the management of these complex pediatric patients and identified important areas for future research.

Keywords: children; home; hypoxemia; oxygen

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This Executive Summary is part of the full official ATS clinical practice guideline, which readers may access online at <http://www.atsjournals.org/doi/abs/10.1164/rccm.201812-2276ST>. Only the Executive Summary is appearing in the print edition of the *Journal*. The article of record, and the one that should be cited, is: Home oxygen therapy for children: an official American Thoracic Society clinical practice guideline. *Am J Respir Crit Care Med* 2019;199:e5–e23.

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This article has an online supplement, which is accessible from this issue's table of contents at www.atsjournals.org.

Am J Respir Crit Care Med Vol 199, Iss 3, pp 270–278, Feb 1, 2019

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DOI: 10.1164/rccm.201812-2276ST

Internet address: www.atsjournals.org

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Summary of Recommendations

Cystic Fibrosis

- For patients with cystic fibrosis complicated by severe chronic hypoxemia, we recommend that home oxygen therapy be prescribed (*strong recommendation, very low-quality evidence*).
- For patients with cystic fibrosis who have both mild chronic hypoxemia and dyspnea on exertion, we suggest that home oxygen therapy be prescribed (*conditional recommendation, very low-quality evidence*).

Bronchopulmonary Dysplasia

- For patients with bronchopulmonary dysplasia complicated by chronic hypoxemia, we recommend that home oxygen therapy be prescribed (*strong recommendation, very low-quality evidence*).

Sleep-disordered Breathing

- For patients with sleep-disordered breathing complicated by severe nocturnal hypoxemia who cannot tolerate positive airway pressure therapy or are awaiting surgical treatment of sleep-disordered breathing, we suggest that home oxygen therapy be prescribed (*conditional recommendation, very low-quality evidence*).

Sickle Cell Disease

- For patients with sickle cell disease complicated by severe chronic hypoxemia, we suggest that home oxygen therapy be prescribed (*conditional recommendation, very low-quality evidence*).

Pulmonary Hypertension without Congenital Heart Disease

- For patients with pulmonary hypertension without congenital heart disease complicated by chronic hypoxemia, we recommend that home oxygen therapy be prescribed (*strong recommendation, very low-quality evidence*).

Pulmonary Hypertension with Congenital Heart Disease

- For patients with pulmonary hypertension with congenital heart disease complicated by chronic hypoxemia, supplemental oxygen will impact hemodynamics and physiology; we recommend that home oxygen therapy NOT be initiated in these children, regardless of previous reparative or palliative congenital heart surgery, until there has been consultation with a pediatric pulmonologist or cardiologist who has expertise in the management of pulmonary hypertension in this clinical setting (*strong recommendation, very low-quality evidence*).

Interstitial Lung Disease

- For patients with interstitial lung disease complicated by severe chronic hypoxemia, we recommend that home oxygen therapy be prescribed (*strong recommendation, very low-quality evidence*).
- For patients with interstitial lung disease who have mild chronic hypoxemia and either dyspnea on exertion or desaturation during sleep or exertion, we suggest that home oxygen therapy be prescribed (*conditional recommendation, very low-quality evidence*).

Implementation

- The expert panel unanimously agreed that optimal implementation of the above recommendations consists of all of the following:
 - Oxygen therapy to maintain an oxygen saturation as measured by pulse oximetry in an acceptable range according to age and respiratory condition as outlined in this document
 - Use of oxygen equipment that is of the appropriate size, developmental stage, and flow rate to function properly
 - Oxygen therapy monitoring by pulse oximetry in the home

Introduction

Home oxygen therapy (HOT) is used to maintain health by addressing physiologic and metabolic requirements for children with chronic lung and pulmonary vascular diseases. Enabling a child to receive HOT also confers psychological advantages by allowing the child to remain within the family unit at home, reducing healthcare costs compared with hospitalization. Despite children having significantly different pulmonary physiology from adults and additional requirements for optimal lung growth and development, indications for funding HOT as determined by the Centers for Medicare and Medicaid Services (CMS) are the same for pediatric and adult patients. These include 1) PaO₂ less than 55 mm Hg (<7.33 kPa), 2) oxygen saturation as measured by pulse oximetry (SpO₂) less than 88%, or 3) PaO₂ 55–59 mm Hg (7.33–7.87 kPa) or SpO₂ 89% accompanied by cor pulmonale, hematocrit greater than 55%, or a history of edema (1). The basis of these indications by CMS is predicated on seminal studies in adult patients with chronic obstructive

pulmonary disease showing reductions in mortality with continuous oxygen therapy (2, 3). Despite the lack of pediatric patients in these historic studies performed over 35 years ago, CMS coverage determination for HOT is the same for pediatric patients of all ages compared with adult patients.

Recognizing the need for clinical guidance regarding HOT specifically for children, the American Thoracic Society (ATS) convened a task force of specialists in pediatric and neonatal medicine, respiratory therapy, nursing, and population health, together with parents, to conduct systematic reviews and use available evidence to inform recommendations for the use of HOT in chronic lung and pulmonary vascular diseases of childhood.

The target audiences of this guideline are clinicians who manage children with diseases complicated by chronic hypoxemia. This group includes pediatric pulmonologists, pediatric cardiologists, neonatologists, general pediatricians and family practitioners, emergency medicine and primary care clinicians, other healthcare professionals, and policy makers. Clinicians, patients, third-party payers, stakeholders, or the courts should never view the recommendations contained in this guideline as dictates. Though evidence-based guidelines can summarize the best available evidence regarding the effects of an intervention in a given patient population, they cannot take into account all of the unique clinical circumstances that may arise when managing a patient, and as such their implementation is at the discretion of each treating clinician.

Methods

This clinical practice guideline was developed in accordance with policies and

procedures of the ATS. See the online supplement for a detailed description of the methods. The meaning of strong and conditional recommendations is described in Table 1. The definition of chronic hypoxemia in a child and the consequences of untreated hypoxemia in this population are included in the online version of the guideline. To define hypoxemia, we conducted a systematic search for data about normal oxygenation in children that identified 1,711 articles, most of which were excluded by review of their title and abstract (see Table E1 in the online supplement). For analysis, we decided to categorize children as those younger than 1 year old or 1 year old and older. See Table 2 for normative values of oxyhemoglobin saturations during wakefulness and sleep in healthy children. For the purpose of this document, the term “desaturation” represents oxyhemoglobin desaturation.

Indications for HOT

Our systematic search of the literature identified 952 articles, most of which were excluded by review of their title and abstract (Table E2). Table 3 provides a summary of the final recommendations by the panel, with details of the evidence base outlined in the following sections for each pediatric respiratory condition.

Question 1: Should Children with Cystic Fibrosis Complicated by Chronic Hypoxemia Be Treated with HOT?

Evidence base. We identified no studies that directly compared home oxygen with no oxygen in children with cystic fibrosis (CF) complicated by chronic hypoxemia, possibly because of concerns about the safety

of having such a control group. We therefore selected eight studies that indirectly addressed the question by comparing use of either short-term oxygen or nocturnal home oxygen with no oxygen in children with CF complicated by chronic hypoxemia (4–11). Seven trials were randomized crossover trials (5–11), and the remaining trial was a randomized trial with parallel groups (4). All trials enrolled children or young adults with both CF (mean age, 22 to 27 yr) and chronic hypoxemia (mean SpO₂ in the mid-80% range; mean PaO₂ <65 mm Hg [<8.67 kPa]; or desaturations to <90%). Three trials compared an FiO₂ of 0.30–0.39 with an FiO₂ of 0.21 administered into the breathing circuit during an exercise test (7, 10, 11); three trials compared an FiO₂ of 0.30–0.31 with an FiO₂ of 0.21 administered by nasal cannula or through a continuous positive airway pressure device during a sleep study (5, 8, 9); one trial compared being in a naturally high oxygen environment below sea level with being at sea level (6); and one trial compared nocturnal HOT titrated to an awake PaO₂ greater than 70 mm Hg (>9.33 kPa) with a nocturnal FiO₂ of 0.21 administered by nasal cannula during sleep. All trials were small, ranging from 6 to 28 patients.

Meta-analyses revealed that short-term oxygen use increased exercise duration (mean difference [MD], +1.04 min; 95% confidence interval [CI], +0.21 to +1.88 min) and postexercise oxygen saturation (MD, +7%; 95% CI, +2.23 to +11.81%); there was also a trend toward a higher peak exercise oxygen saturation (MD, +7.19%; 95% CI, –2.51% to +16.89%). Single studies revealed that short-term oxygen use mitigated oxygen desaturation during exercise (–5% vs. –12%; MD, +7%; 95% CI, +2.48% to +11.52%) (12), improved oxygen saturation during REM sleep (90% vs. 79%; MD, +11%; 95% CI, +4.38% to +17.62%) and non-REM (NREM) sleep

Table 1. Meanings of the Strength of the Recommendations

A Strong Recommendation Conveys . . .	A Conditional Recommendation Conveys . . .
It is the right course of action for >95% of patients.	It is the right course of action for >50% of patients but may not be right for a sizable minority.
“Just do it. Don’t waste your time thinking about it, just do it.”	“Slow down, think about it, discuss it with the patient.”
You would be willing to tell a colleague that he or she did the wrong thing if he or she did not follow the recommendation.	You would NOT be willing to tell a colleague that he or she did the wrong thing if he or she did not follow the recommendation because there is clinical equipoise.
The recommended course of action may make a good performance metric.	The recommended course of action would NOT make a good performance metric.

Table 2. Normative Values

	Wakefulness		Sleep		Desaturation Nadir	
	Mean (±SD)	Median (Range)	Mean (±SD)	Median (Range)	Mean (±SD)	Median (Range)
Children <1 yr old	97.8% (±1.4%)	98.7% (97.9–99.8%)	96.3% (±1.3%)	Not reported	86% (±1.5%)	85.5% (83–88%)
Children ≥1 yr old	97.6% (±0.7%)	97.5% (97–98%)	97.8% (±0.7%)	Not reported	94.6% (±3.1%)	93% (91–94%)

(94% vs. 88%; MD, +6%; 95% CI, +1.36% to +10.64%) (9), reduced sleep latency (18 vs. 24 min; MD, -6 min; 95% CI, -0.25 to -11.75 min) (9), and improved school attendance at 6 months (71% vs. 21%; relative risk, 3.3; 95% CI, 1.16 to 9.59) and 12 months (91% vs. 20%; relative risk, 4.55; 95% CI, 1.30 to 15.9) (4). There were trends toward more REM sleep time (18% vs. 13%; MD, +6%; 95% CI, -0.93% to +12.93%) and a lower arousal index (6 vs. 8.1 arousals/h; MD, -2.1 arousals/h; 95% CI, -4.57 to +0.37 arousals/h). There were no differences in mortality (4), growth (4), total sleep time (9), respiratory function (4), or right ventricular function (4).

The panel had very low confidence that the estimated effects described above would be the same for HOT in patients with CF complicated by chronic hypoxemia, because the evidence from which the estimates were derived was indirect (i.e., the question was about HOT, but the estimates were from trials that used short-term oxygen or nocturnal HOT) and the trials were all small with few events.

Conclusions. Despite having very low confidence in the estimated effects, the panel was certain that the benefits of HOT exceed the harms, burdens, and cost in patients with CF with severe chronic hypoxemia ($Sp_{O_2} < 90\%$). This was based on the large number of beneficial outcomes and absence of harmful outcomes, decades of clinical experience collectively managing thousands of such patients, and recognition that prolonged chronic hypoxemia contributes to serious health consequences such as pulmonary hypertension (PH) and cor pulmonale. The panel also concluded that the benefits of HOT likely exceed the harms, burden, and cost in patients with CF who have mild hypoxemia (Sp_{O_2} 90–93%) that is chronic, accompanied by sequelae of hypoxemia (e.g., dyspnea on exertion, PH, cor pulmonale), or that occurs in the

context of an exacerbation requiring antibiotics.

ATS recommendations.

- **For patients with CF complicated by severe chronic hypoxemia, we recommend that HOT be prescribed** (*strong recommendation, very low-quality evidence*). Severe chronic hypoxemia is defined as either 1) greater than or equal to 5% of recording time spent with an Sp_{O_2} less than 90% if measurements are obtained by continuous recording or 2) at least three separate findings of an Sp_{O_2} less than 90% if measurements are obtained intermittently.
- **For patients with CF who have both mild chronic hypoxemia and dyspnea on exertion, we suggest that HOT be prescribed** (*conditional recommendation, very low-quality evidence*). Mild chronic hypoxemia is defined as either 1) greater than or equal to 5% of recording time spent with an Sp_{O_2} 90–93% if measurements are obtained by continuous recording or 2) at least three separate findings of an Sp_{O_2} 90–93% if measurements are obtained intermittently.

Question 2: Should Children with Bronchopulmonary Dysplasia Complicated by Chronic Hypoxemia Be Treated with HOT?

Evidence base. We identified 11 observational studies that compared HOT with no oxygen therapy in children whose bronchopulmonary dysplasia (BPD) was complicated by chronic hypoxemia. Ten of the studies were excluded because there was an unacceptable risk of bias owing to the patients receiving HOT being more severely ill than the patients in the no-oxygen group. The remaining study was selected for analysis (13).

The study enrolled 63 infants with BPD who were receiving HOT but had an Sp_{O_2} greater than or equal to 92% in room air. The infants were admitted for continuous

pulse oximetry in room air during sleep and then categorized into three groups: those who 1) maintained an Sp_{O_2} greater than or equal to 92%, 2) had desaturations to 88–91% for more than 1 hour, or 3) had desaturations to less than 88% for more than 1 hour. Those who maintained an Sp_{O_2} greater than or equal to 92% or had desaturations to 88–91% had their supplemental oxygen discontinued, whereas those who had desaturations to less than 88% had their supplemental oxygen continued. For the groups whose oxygen was discontinued, various growth parameters were measured before and after discontinuation of oxygen and compared. Because the issue being addressed concerns children with chronic hypoxemia, our analysis focused on the 14 infants who had desaturations to 88–91% during sleep. The study revealed that the rate of weight gain was greater while the infants were receiving supplemental oxygen than after discontinuation (15.9 g/kg/d vs. 3.7 g/kg/d; MD, 12.2 g/kg/d; 95% CI, 7.22 to 17.18 g/kg/d).

The panel supplemented this study with indirect evidence. Two studies enrolled patients with BPD who had ongoing high oxygen requirements: one compared hemodynamics measured by right heart catheterization during the inhalation of 80% oxygen for 10 minutes with those measured during the inhalation of room air for 10 minutes (14), whereas the other compared hemodynamics measured during the inhalation oxygen targeting a Pa_{O_2} greater than 120 mm Hg (>16 kPa) with those measured during the inhalation oxygen targeting a Pa_{O_2} of 55 to 120 mm Hg (7.33–16 kPa) (15). Meta-analysis found that oxygen administration was associated with lower mean pulmonary artery pressure (MD, -10.03 mm Hg [-1.34 kPa]; 95% CI, -16.41 to -3.64 mm Hg [-2.19 to -0.49 kPa]). Another study enrolled patients with BPD who required oxygen to keep their Sp_{O_2} above 90% and compared polysomnography results while subjects breathed either an extra 0.25 L/min of

Table 3. Summary of Recommendations for Home Oxygen Therapy in Children with Strength of the Recommendation and Level of Evidence

Pediatric Respiratory Condition	Recommendation	Strength of Recommendation and Level of Evidence
Cystic fibrosis	For patients with cystic fibrosis complicated by severe chronic hypoxemia, we recommend that home oxygen therapy be prescribed. For patients with cystic fibrosis who have both mild chronic hypoxemia and dyspnea on exertion, we suggest that home oxygen therapy be prescribed.	Strong recommendation, very low-quality evidence Conditional recommendation, very low-quality evidence
Bronchopulmonary dysplasia	For patients with bronchopulmonary dysplasia complicated by chronic hypoxemia, we recommend that home oxygen therapy be prescribed.	Strong recommendation, very low-quality evidence
Sleep-disordered breathing	For patients with sleep-disordered breathing complicated by severe nocturnal hypoxemia who cannot tolerate positive airway pressure therapy or are awaiting surgical treatment of sleep-disordered breathing, we suggest that home oxygen therapy be prescribed.	Conditional recommendation, very low-quality evidence
Sickle cell disease	For patients with sickle cell disease complicated by severe chronic hypoxemia, we suggest that home oxygen therapy be prescribed.	Conditional recommendation, very low-quality evidence
Pulmonary hypertension without congenital heart disease	For patients with pulmonary hypertension without congenital heart disease complicated by chronic hypoxemia, we recommend that home oxygen therapy be prescribed.	Strong recommendation, very low-quality evidence
Pulmonary hypertension with congenital heart disease	For patients with pulmonary hypertension with congenital heart disease complicated by chronic hypoxemia, supplemental oxygen will impact hemodynamics and physiology; we recommend that home oxygen therapy NOT be initiated in these children, regardless of previous reparative or palliative congenital heart surgery, until there has been consultation with a pediatric pulmonologist or cardiologist who has expertise in the management of pulmonary hypertension in this clinical setting.	Strong recommendation, very low-quality evidence
Interstitial lung disease	For patients with interstitial lung disease complicated by severe chronic hypoxemia, we recommend that home oxygen therapy be prescribed. For patients with interstitial lung disease who have mild chronic hypoxemia and either dyspnea on exertion or desaturation during sleep or exertion, we suggest that home oxygen therapy be prescribed.	Strong recommendation, very low-quality evidence Conditional recommendation, very low-quality evidence

supplemental oxygen or their baseline amount of oxygen (16). The higher amount of oxygen was associated with increased total sleep duration, increased REM sleep duration, and decreased REM arousals, although the values of each were not reported.

The panel had very low confidence that the estimated effects described above are the same for HOT in patients with BPD

complicated by chronic hypoxemia. The direct evidence was derived from a single, small observational study. The indirect evidence derived estimates from small observational studies that used short-term oxygen or nocturnal HOT rather than HOT.

Conclusions. The panel emphasized that patients with chronic hypoxemia due to

BPD generally reach a phase in their medical care where they face two alternatives: receive long-term oxygen in the hospital or at home. This occurs when other medical issues have stabilized but altered oxygenation levels are only slowly improving. The panel was certain, despite its very low confidence in the estimated effects, that the benefits of HOT exceed the harms, burdens, and cost.

In addition to improved growth, lower pulmonary artery pressure, improved sleep duration, and fewer arousals from sleep, HOT enables the patient and family to be at home and diminishes the likelihood of harm by preventing the nosocomial and iatrogenic consequences of hospitalization. The strength of the panel's recommendation is strong because its primary intention is to prevent the harmful effects of prolonged hospitalization.

ATS recommendation.

- **For patients with BPD complicated by chronic hypoxemia, we recommend that HOT be prescribed** (*strong recommendation, very low-quality evidence*). Chronic hypoxemia is defined as either 1) greater than or equal to 5% of recording time spent with an SpO₂ less than or equal to 93% if measurements are obtained by continuous recording or 2) at least three separate findings of an SpO₂ less than or equal to 93% if measurements are obtained intermittently.

Question 3: Should Children with Sleep-disordered Breathing Complicated by Chronic Hypoxemia Be Treated with HOT?

Evidence base. We identified two studies that compared nocturnal oxygen with no oxygen therapy in children with sleep-disordered breathing (SDB) complicated by nocturnal hypoxemia (17, 18). One study was a randomized crossover trial that enrolled children (mean age, 5 yr) who had suspected obstructive sleep apnea plus desaturation during sleep to less than 92% (17); the other study was an observational study that enrolled children (mean age, 4.3 yr) who had tonsillar hypertrophy and desaturations during sleep to less than 90% (18). Both studies compared the effects of supplemental oxygen with room air during sleep; one study provided oxygen at a rate of 1 L/min (17), and the other provided oxygen at a rate needed to keep the patient's SpO₂ above 95% (18).

The apnea index was the only outcome measured by both studies; when pooled by meta-analysis, oxygen use during sleep was associated with no change in the apnea index (MD, -3 events/h; 95% CI, -12.92 to +6.68 events/h). In single studies, oxygen use during sleep was also associated with a higher mean SpO₂ (MD, +8.2%; 95% CI, +5.58% to +10.82%), nadir SpO₂ (MD, +20.7%; 95% CI, +11.29%

to +30.11%), and nadir SpO₂ during REM sleep (MD, +9%; 95% CI, +1.57% to +16.43%). It was associated with trends toward a higher mean SpO₂ during REM sleep (MD, +4%; 95% CI, -0.16% to +8.16%), mean SpO₂ during NREM sleep (MD, +3%; 95% CI, -0.39% to +6.39%), and nadir SpO₂ during NREM sleep (MD, +4%; 95% CI, -0.47% to +8.47%). There was no difference in the hypopnea index (MD, -3.8 events/h; 95% CI, -19.32 to +11.72 events/h) or changes in overall end-tidal PCO₂ levels, although PCO₂ increased significantly in a few patients.

The panel's confidence in the accuracy of these estimated effects in the patient population of interest to them was very low. There was indirectness of the intervention because the question is about HOT provided chronically at night, but the studies used oxygen provided during a single night. There was also indirectness of outcomes because those assessed were all short-term physiologic measures rather than the long-term clinical outcomes that the panel would have preferred. In addition, the studies were small, and there was a risk of bias, because neither study reported enrolling consecutive patients and one study was not blinded.

Conclusions. The panel concluded that the benefits of HOT likely exceed the harms, burdens, and cost for the majority of patients with severe nocturnal hypoxemia due to SDB who either cannot tolerate positive airway pressure therapy or are awaiting surgical treatment of their SDB. Although the studies above merely show that giving oxygen increases oxygenation, there is abundant evidence that improving nocturnal oxygenation by other means, such as positive airway pressure, mitigates adverse cardiopulmonary consequences of nocturnal hypoxemia in children. The panel had no reason to suspect that relief of nocturnal hypoxemia by oxygen or positive airway pressure will lead to different consequences.

ATS recommendation.

- **For patients with SDB complicated by severe nocturnal hypoxemia who cannot tolerate positive airway pressure therapy or are awaiting surgical treatment of SDB, we suggest that HOT be prescribed** (*conditional recommendation, very low-quality evidence*). Severe nocturnal hypoxemia is defined as greater than or equal to 5% of

recording time spent with an SpO₂ less than 90% during sleep.

Question 4: Should Children with Sickle Cell Disease Complicated by Chronic Hypoxemia Be Treated with HOT?

Evidence base. Many reported associations between hypoxemia and outcomes such as stroke and pain crises, but they were excluded because they did not compare use of oxygen with no oxygen therapy. We identified two observational studies that evaluated patients before, during, and after receiving supplemental oxygen (19, 20). Both studies enrolled patients with sickle cell disease (SCD), but neither reported the ages of the patients or the degree of chronic hypoxemia. One study of three patients administered oxygen at 5 L/min by nasal prongs (19), whereas the other study of four patients administered 70–100% oxygen continuously for 8 to 20 days (20).

Measures of oxygenation increased during oxygen therapy. In one study, the PaO₂ ranged from 72 to 83 mm Hg (9.60 to 11.07 kPa) before receiving supplemental oxygen and 146 to 175 mm Hg (19.47 to 23.33 kPa) while receiving oxygen (19). In the other study, which reported a single representative patient only, the SpO₂ was 89% before the initiation of oxygen, 100% during administration, and 83% after discontinuation (20). In both studies, the number and percentage of sickle cells decreased during oxygen administration, although this was not accompanied by less hemolysis. The amount of sickle cells rebounded when the oxygen was discontinued, with six of seven patients rebounding to higher-than-baseline levels and the remaining patient rebounding to baseline levels (19, 20). One study was terminated early because two of three patients developed pain crises after discontinuation of the supplemental oxygen, although none of the four patients in the other study experienced a pain crisis (19).

The panel's confidence in the accuracy of these estimated effects in the patient population of interest to them was very low. There was indirectness of the intervention because the oxygen was provided at much higher levels than current norms. In addition, there was a risk of bias for multiple reasons: the studies were not blinded, did not report enrolling consecutive patients, and

did not report all of the data that were collected.

Conclusions. The panel acknowledged that the studies described above raise serious concerns about the potential for harm if oxygen is discontinued in patients with SCD. However, the panel had very low confidence in the findings, owing to the studies' small size (only seven patients total) and publication age (cointerventions were different in 1944 and 1984).

Moreover, the panel has collectively used oxygen in hundreds of patients with SCD for a variety of reasons without increases in sickle cell crises or acute chest syndrome upon discontinuation, and it was concerned about the untoward effects of allowing severe chronic hypoxemia to go unabated.

ATS recommendation.

- **For patients with SCD complicated by severe chronic hypoxemia, we suggest that HOT be prescribed** (*conditional recommendation, very low-quality evidence*). Severe chronic hypoxemia is defined as either 1) greater than or equal to 5% of recording time spent with an Sp_{O₂} less than 90% if measurements are obtained by continuous recording or 2) at least three separate findings of an Sp_{O₂} less than 90% if measurements are obtained intermittently.

Question 5: Should Children with Pulmonary Hypertension without Congenital Heart Disease Be Treated with HOT?

Evidence base. We identified no studies that compared the effects of HOT with no oxygen therapy in children with PH complicated by chronic hypoxemia. The panel discussed whether to review indirect evidence from adults but judged adults with PH to be too indirect a population to inform recommendations in children. Instead, the panel decided to inform its recommendations with their collective nonsystematic clinical observations derived from caring for many such patients over several decades. Nonsystematic clinical observations give very low confidence in the estimated effects.

Conclusions. The panel emphasized that empirical evidence comparing HOT with no oxygen therapy will never be forthcoming, because withholding HOT in such patients is ethically questionable. The panel's collective clinical experience suggests that children with chronic hypoxemia due to PH are less dyspneic and more active

when receiving HOT. Although harmful consequences of HOT are infrequent, there can be effects on quality of life. Most important, the panel was particularly certain about the potential of HOT to benefit patients by mitigating the undesirable consequences of chronic hypoxemia because it directly interrupts the vicious cycle of PH causing hypoxemia, which in turn worsens the PH.

ATS recommendation.

- **For patients with PH without congenital heart disease complicated by chronic hypoxemia, we recommend that HOT be prescribed** (*strong recommendation, very low-quality evidence*). Chronic hypoxemia is defined as either 1) greater than or equal to 5% of recording time spent with an Sp_{O₂} less than or equal to 93% if measurements are obtained by continuous recording or 2) at least three separate findings of an Sp_{O₂} less than or equal to 93% if measurements are obtained intermittently.

Question 6: Should Children with Pulmonary Hypertension with Congenital Heart Disease Be Treated with HOT?

Evidence base. We identified no studies that compared the effects of HOT with no oxygen therapy exclusively in children with congenital heart disease (CHD). The only relevant study was a nonrandomized trial of supplemental oxygen for patients with PH, in which 13 of the 15 patients had CHD (21). Nine patients were assigned to receive HOT for at least 12 hours per day, and six patients were assigned no HOT. The patients were followed for up to 5 years. Baseline values revealed a trend toward higher Sp_{O₂} in the HOT group (+5%; -4.43% to +14.43%), a trend toward lower pulmonary vascular resistance in the HOT group (-7 mm Hg/min/m²/L; 95% CI, +3.67 to -17.67 mm Hg/min/m²/L), and no difference in the pulmonary artery pressure. Mortality was lower among children who received HOT (0% vs. 83%; relative risk not estimable). Exercise capacity and symptoms were reportedly measured by questionnaire, but the results were not described. The study provided very low confidence in its estimated effects.

Conclusions. The panel acknowledged that the evidence favored HOT but had very low confidence in the estimated effects,

owing to the study design, potential bias, and imprecision. They also expressed concern that in some patients with unrepaired CHD and significant left-to-right shunt, increased pulmonary blood flow can be harmful rather than beneficial. Generally speaking, they strongly believed that the fine balance between the potential for either beneficial or harmful effects dictates that such patients be evaluated and treated by clinicians with experience in managing such complicated patients. In children with surgically repaired CHD, however, concerns of high pulmonary blood flow would not persist, and the effects of oxygen therapy to avoid hypoxemia, especially in the setting of PH, are likely greater than potential adverse effects.

ATS recommendation.

- **For patients with PH with CHD complicated by chronic hypoxemia, supplemental oxygen will impact hemodynamics and physiology; we recommend that HOT NOT be initiated in these children, regardless of previous reparative or palliative congenital heart surgery, until there has been consultation with a pediatric pulmonologist or cardiologist who has expertise in the management of PH in this clinical setting** (*strong recommendation, very low-quality evidence*).

Question 7: Should Children with Interstitial Lung Disease Complicated by Chronic Hypoxemia Be Treated with HOT?

Evidence base. We identified no studies that compared the effects of HOT with no oxygen therapy in children with interstitial lung disease (ILD) complicated by chronic hypoxemia. The panel discussed whether to review indirect evidence from adults but judged adults with ILD to be too indirect a population to inform recommendations in children. Instead, the panel decided to inform its recommendations with their collective nonsystematic clinical observations. Nonsystematic clinical observations give very low confidence in the estimated effects.

Conclusions. The panel again emphasized that empirical evidence comparing oxygen use with no oxygen therapy will never be forthcoming, because withholding HOT in such patients is ethically questionable. The panel was certain that the benefits of HOT exceed the harms,

burdens, and cost in patients with ILD with severe chronic hypoxemia (SpO₂ <90%). This was based on the large number of beneficial outcomes that they have observed in their clinical practices and the absence of harmful outcomes, decades of clinical experience in managing many such patients, and recognition that prolonged chronic hypoxemia can contribute to serious health consequences such as PH and cor pulmonale. The panel also concluded that the benefits of HOT likely exceed the harms, burden, and cost in patients with ILD who have mild hypoxemia (SpO₂ 90–93%) that is chronic, accompanied by sequelae of hypoxemia (e.g., dyspnea on exertion), or associated with desaturation during sleep or exertion.

ATS recommendations.

- **For patients with ILD complicated by severe chronic hypoxemia, we recommend that HOT be prescribed** (*strong recommendation, very low-quality evidence*). Severe chronic hypoxemia is defined as either 1) greater than or equal to 5% of recording time spent with an SpO₂ less than 90% if measurements are obtained by continuous recording or 2) at least three separate findings of an SpO₂ less than 90% if measurements are obtained intermittently.
- **For patients with ILD who have both mild chronic hypoxemia and either dyspnea on exertion or desaturation during sleep or exertion, we suggest that HOT be prescribed** (*conditional*

recommendation, very low-quality evidence). Mild chronic hypoxemia is defined as either 1) greater than or equal to 5% of recording time spent with an SpO₂ 90–93% if measurements are obtained by continuous recording or 2) at least three separate findings of an SpO₂ 90–93% if measurements are obtained intermittently.

Providing HOT

Evidence-based data that address the optimal modalities of home oxygen delivery and monitoring in the pediatric population are limited. Although an in-depth discussion of specific delivery and monitoring methods is beyond the scope of this guideline, panel members identified important considerations for equipment choice, including the patient’s age, size, and developmental stage, as well as the required flow rate. Furthermore, equipment choices should remain under appropriate supervision. Owing to space limitations, this section is completed in the online version.

Discontinuation of HOT

Although some conditions may warrant indefinite HOT, improvements in respiratory function that occur with age, maturation, treatment, clinical course, and

so forth can lead to an opportunity to wean (progressively decrease) or discontinue (stop altogether) HOT. Improvements in respiratory status amenable to weaning of oxygen therapy are most applicable to infants with chronic lung disease of prematurity, but a standardized approach may nonetheless be helpful in other populations. Criteria for the justification and initiation of HOT are outlined by CMS, but weaning or discontinuation is not. Owing to space limitations, this section is completed in the online version.

Conclusions

Despite widespread use of HOT in children for various lung and pulmonary vascular diseases, there is a striking paucity of data regarding its implementation, efficacy, monitoring, and discontinuation. With limited evidence, the panel provides recommendations based on expert opinion and experiences associated with patient-important outcomes that will aid clinicians in the management of complex pediatric patients requiring HOT. Future research should address important areas including SpO₂ levels associated with optimal growth and development and the identification of best practice for weaning and discontinuing HOT in children. ■

This official clinical practice guideline was prepared by an *ad hoc* subcommittee of the ATS Assembly on Pediatrics.

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Author Disclosures: R.R.D. served on an advisory committee for Boehringer Ingelheim

and ListenMD; served as a speaker for Novartis; received royalties from Elsevier Publishing; held a patent for a Personalized Health Care Wearable Sensor System; had patents pending for Systems and Methods for Determining Vital Information with a Computing Device, for a Pediatric Nasal Endoscope, for a Respiration Rate Measurement System, and for a Tongue Localization, Teeth Interaction, and Detection System; served as consultant for, and had ownership or investment interests and other intellectual property with, TripleEndoscopy Inc.; and had ownership or investment interests and royalties, licensing fees, or other sales proceeds with Now Vitals Inc. S.H.A. received research support from Shire Pharmaceuticals and United Therapeutics; and served on an advisory committee for Shire Pharmaceuticals. M.E.C. served as editor-in-chief for and received an honorarium from *Pediatric Allergy, Immunology, and Pulmonology*; served as an associate editor for the *American Academy of Pediatrics, Pediatric Pulmonology: A Manual for Primary Care*; and served as an

editor for *StatPearls*. R.J.M. served on a data safety monitoring board for CareFusion and Windtree Therapeutics. H.B.P. served on an advisory committee for Philips Respirronics; and received royalties from UpToDate. K.C.W. reported employment by the American Thoracic Society as Chief of Documents and Patient Education and Documents Editor and derived salary support from these roles, and as such he has a personal financial interest in the quality of all ATS clinical practice guidelines. D.H., J.B., I.M.B.-L., C.L.C., A.G., D.G., S.M.M.H., T.M.H., D.K., K.K., G.K., E.O., G.R.P., L.M.R., M.L.S., and D.T. reported no relationships with relevant commercial interests.

Acknowledgment: This official document was prepared by a subcommittee of the Assembly on Pediatrics. The members of the clinical practice guideline panel on home oxygen therapy for children thank Kimberly Lawrence for the excellent and thoughtful job she did in organizing this panel, which was invaluable for the generation of this document.

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